Case study

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Uterine diseases of captive large felids in Malaysia: seven clinical case reports

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Abstract

Background Captive large felids are at risk of various uterine diseases that include pyometra, hematometra, and neoplasms (leiomyoma and adenocarcinoma).

Objective This case study aimed to describe seven cases of female uterine diseases were diagnosed in three zoos and one wildlife rescue center over nine years in Malaysia.

Case Description The cases diagnosed were on three Malayan tigers (*Panthera tigris jacksoni*), a white Bengal tiger (*P. tigris tigris*), two white lions (*P. leo*), and a common leopard (*P. pardus*). Diagnosis was made based on clinical signs, blood tests (complete blood counts and serum biochemistry), abdominal radiographs, ultrasonography, laparoscopy, cytology, and histopathology (post-mortem).

Medical Management Treatments included ovariohysterectomy, systemic antibiotics, analgesics, hormones, and fluid therapy. The outcomes in these cases varied.

Conclusion The most common clinical signs seen in these seven cases were vulvar discharge, inappetence, and lethargy. Common blood findings were neutrophilia, leukocytosis, and hyperproteinemia due to hyperglobulinemia. Abdominal radiographs were generally non-specific, revealing radiopaque structures within the abdomen. Ultrasonography revealed a distended and fluid/mass-filled uterus. Reproductive evaluation of large captive felids should be included in annual health checks as the females age.

Keywords large felids | *Panthera* sp. | pyometra | reproductive organ | uterine diseases

Introduction

In general, the anatomy of the female reproductive tract consists of the vulva, vagina, cervix, uterus, oviduct, and ovaries. Oviducts are also known as fallopian tubes, which connect the ovaries to the uterus. The end of the uterus, known as the cervix, separates the uterus from the vagina. The vagina is a muscular tube that extends from the uterus to the vulva, which is the external opening of the female reproductive organs/genitals (Momont, 2018).

The most commonly reported uterine disease in small animals is pyometra, an accumulation of pus in the uterus that is common in intact female dogs and cats. This disease is usually secondary to an acute or chronic suppurative bacterial infection of the uterus, as well as cystic endometrial hyperplasia (CEH) (Hagman, 2018; McCain *et al.*, 2009). According to Hagman (2018), hormones, especially progesterone, play an important role during the luteal phase, allowing opportunistic bacteria to establish an ascending infection that leads to the development of this disease.

In contrast, hematometra is a pathological condition in which blood accumulates in the uterus. This condition is uncommon during presentation, especially in small animals. To the best of our knowledge, this is the first report of a hematometra-pyometra complex in a large felid. There are many

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differential diagnoses and possible etiologies of haematometra. These include postpartum endometritis, serosal inclusion cysts, uterine tumors, rodenticide toxicity, and uterine trauma (Troxel *et al*, 2002).

The most common uterine neoplasm reported in large older felids is leiomyoma (Junginger *et al*, 2015). Leiomyomas are benign smooth muscle tumors (Gadhave *et. al*, 2019). Uterine adenocarcinoma is the most common uterine neoplasm in domestic cats (Miller *et al*, 2002). However, they are still considered rare in domestic animals, except for rabbits and cows. Adenocarcinoma is a malignant epithelial tumor that arises from the endometrium.

Case Description and Treatment

Sunway Lagoon Wildlife Park

Case 1

Asha is an 8-year-old female white Bengal tiger (*Panthera tigris tigris*) managed in captivity in Sunway Lagoon Wildlife Park. The animal was housed with a male conspecific. The tiger was found to be weak in its night stall one morning, with acute bloody vulvar discharge with the presence of mucus (**Figure 1A**). Immediate general anesthesia was achieved with a combination of ketamine (Narketan®-10, Vetoquinol, UK, 2.5 mg/kg) and xylazine HCL (Ilium Xylazil®, Troy Lab, Australia, 0.5 mg/kg).
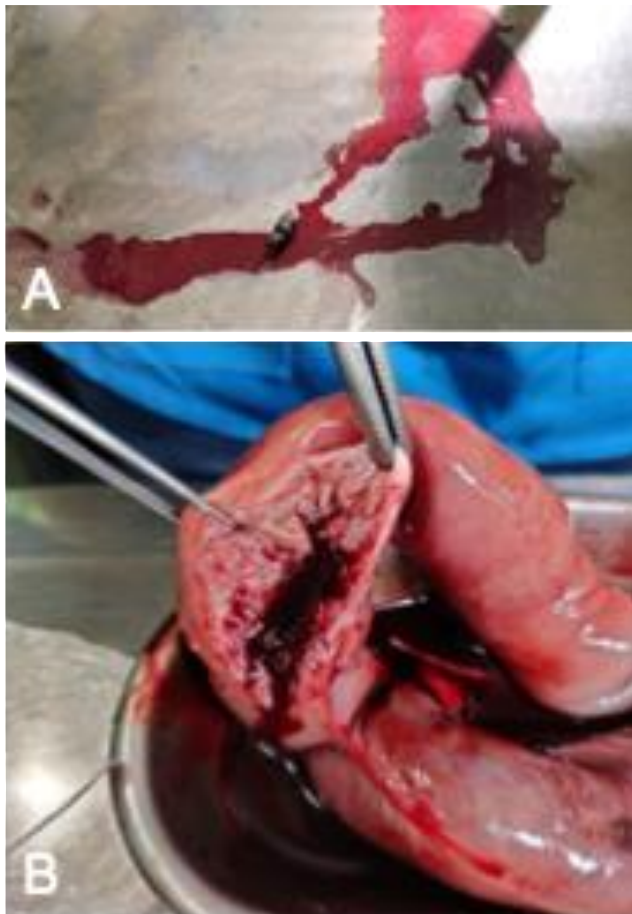

Figure 1 Clinical symptoms observed in Asha, an 8-year-old female white Bengal tiger (*Panthera tigris tigris*) managed in Sunway Lagoon Wildlife Park. (A) Bloody mucoid vulvar discharge found at the night stall floor; (B) Bloody uterus with a thickened uterine wall.

Blood samples for complete blood count (CBC), serum biochemistry (BioChem), and uterine swabs were collected (**Table 1**). The tiger was administered enrofloxacin at a dosage of 5 mg/kg, meloxicam at a dosage of 0.2 mg/kg, and an iron supplement was administered alongside intravenous fluid therapy (lactated Ringer solution and Duphalyte®) at a rate of 10 ml/kg/hr. The CBC and BioChem revealed neutrophilic leukocytosis with lymphopenia, high packed cell volume (PCV) and hemoglobin counts, thrombocytopenia, hypoglycemia, low blood urea nitrogen (BUN) levels, hyperproteinemia, hyperglobulinemia, and high levels of creatinine, alanine transaminase (ALT), amylase, and lipase.

The animal's condition showed minor improvements in the amount of bloody mucoid discharges from the vulva, but the tiger developed vomiting and diarrhea and remained dull and inappetent. Metoclopramide, amoxicillin trihydrate, vitamin K, and ranitidine were also added to the treatment regimen. Electrolytes, glucose powder, and multivitamins were added to drinking water. Cloprostenol (a prostaglandin F2 alpha analog) at a dosage of 1µg/kg was given subcutaneously to promote uterine emptying.

A ventral midline ovariohysterectomy was performed, and a thick, blood-filled uterus with abnormal ovaries was removed (**Figure 1B**). Histopathological examination confirmed the presence of ulcerative endometritis and polycystic ovaries. Unfortunately, the animal died 4 days after surgery.

Case 2

Zuri is an 8-year-old female white lion (*Panthera leo*) managed in captivity in Sunway Lagoon Wildlife Park. The animal was housed with a male conspecific. Droplets of milky caseous and watery discharges were observed in the night stall (**Figure 2A**). Clinical signs such as hyporexia, dullness, and vomiting were observed during monitoring. Swab samples of the vulvular discharge were obtained and subjected to bacterial culture and antibiotic sensitivity tests (**Table 1**). The lion was started on amoxicillin and clavulanic acid at a dosage of 15 mg/kg. To perform further examinations, general anesthesia was administered. General anesthesia was achieved with a combination of ketamine (Narketan®-10, Vetoquinol, UK,1.6 mg/kg), xylazine HCL (Ilium Xylazil®, Troy Lab, Australia, 0.4 mg/kg), and tiletamine zolazepam (Zoletil®, Virbac, Australia, 1.15 mg/kg).

An abdominal ultrasound service was performed by the radiology team from the University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM). The scan revealed a fluid-filled tubular structure with a diameter of ~3 cm (**Figure 2B**). Vaginal swab samples were collected for cytology, bacterial culture, and antibiotic sensitivity testing (**Table 1**). Blood samples were also taken for CBC and BioChem, which revealed leukocytosis with neutrophilia and monocytosis. The animal was started on marbofloxacin at a dose of 8 mg/kg after the results of the 2nd culture and received a dose of cloprostenol (prostaglandin F2 alpha analog) at a dosage of 1µg/kg. She also received a single dose of liver supplement, Catosal®, and ivermectin. Alternate-day doses of meloxicam at a dosage of 0.2 mg/kg were also prescribed. Vaginal discharges were observed in larger quantities and
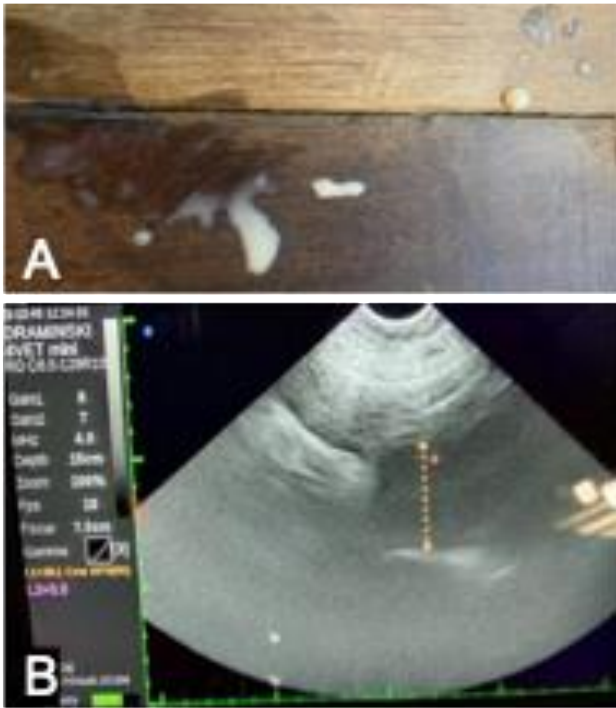
Figure 2 Clinical evidence observed in Zuri, an 8-year-old female white lion (*Panthera leo*) managed in Sunway Lagoon Wildlife Park. (A) Caseous discharge at the night stall floor; (B) Fluid-filled tubular structure observed by abdominal ultrasonography.

were slightly bloody for 2-3 days after prostaglandin administration. Discharges stopped, and the lioness appeared more alert and showed no clinical signs thereafter.

Eight months later, the female lioness was observed with whitish vulvular discharges again at night stall; however, appetite and behavior were normal. A similar treatment protocol was started with Marbofloxacin (Forcyl, Vetoquinol, Spain, 8 mg/kg) and a dose of cloprostenol (Cloprostenol, Vemedim, Vietnam, 1µg/kg). The discharges cleared in two days.

After four months, the female lioness was observed with similar clinical signs: whitish vulvular discharges. A similar treatment protocol was administered with marbofloxacin (Forcyl, Vetoquinol, Spain, 8 mg/kg) and a dose of cloprostenol (Cloprostenol, Vemedim, Vietnam, 1µg/kg). In this episode, whitish vulvular discharges were persistently observed for one week. Hence, the second dose of cloprostenol (Cloprostenol, Vemedim, Vietnam, 1µg/kg) was administered. The whitish vulvular discharge ceased the following day.

One month later, hysteroscopy and uterine flushing were performed, assisted by the Department of Wildlife and National Parks (PERHILITAN) and Universiti Putra Malaysia (UPM). Unfortunately, the cervix was not fully relaxed during the procedure, and uterine flushing was unsuccessful. Nine days later, a recurrent episode of whitish vulvular discharge occurred. A similar treatment protocol with marbofloxacin (Forcyl, Vetoquinol, Spain; 8 mg/kg) and cloprostenol (Cloprostenol, Vemedim, Vietnam, 1µg/kg) was administered. On the following day, the discharge was cleared.

Eleven months later, a second hysteroscopy and uterine flushing were performed. In this round, 48 hours before general anesthesia, the lioness was darted with a dose of cloprostenol (Cloprostenol, Vemedim, Vietnam, 1µg/kg) to allow muscle relaxation of the cervix. The second dose was administered intraoperatively, and uterine flushing was successfully performed. No discharges were observed, and a subsequent ultrasound examination revealed a normal appearance of the uterine body.

Zoo Melaka
Case 3

Lala is a 5-year-old female white lion (*Panthera leo*) managed in captivity in Zoo Melaka, reported with clinical signs of inappetence three days before parturition and continued eight days post-parturition. The lioness gave birth to two live cubs within a 2-hour interval. Both cubs were active, but suckling was observed only after 6 hours.

Antibiotic therapy was initiated on day three post-parturition with marbofloxacin (Marbocyl®10%, Vetoquinol, UK, 2.75 mg/kg) and amoxicillin (Betamox LA®, Norbrook 150, 15 mg/kg) for 5 days alongside anti-inflammatory meloxicam (Melonex®, Intas Pharmaceuticals Ltd., India, 0.2 mg/kg). During the next few days, the lioness expelled four dead fetuses, had dark, foul-smelling vaginal discharge, and spent most of the day on lateral recumbency. A single dose of cloprostenol (Estrumate®, Coopers Animal Health, Australia, 1 µg/kg) to encourage expulsion of dead fetuses and discharge was administered.

Due to deteriorating conditions, general anesthesia was administered on day eight post-parturition. With assistance from PERHILITAN and UPM, the lioness was sedated with xylazine (Chanazine® 10%, Chanelle Pharma, Ireland, 2 mg/kg), 3mL, IM, and Ketamine (Ilium Ketamil® 100 mg/ml, Troy Lab, Australia, 5.5 mg/kg). The animal was placed in the right lateral recumbent position. A sterile swab was used to collect the discharge from the vagina for cytology and bacterial culture (**Table 1**). Blood samples were collected via venipuncture for complete blood count and serum biochemistry analysis, which revealed neutrophilia and monocytosis suggestive of early infection, while serum biochemistry revealed increased creatinine levels with increased globulin. The ventral abdomen and inguinal region were cleaned with diluted chlorhexidine and water to remove debris and discharge. Cellulitis was observed around the inguinal area, probably due to prolonged urine and discharge in contact with the skin (**Figure 3A**).

A dog catheter size 10FR was inserted into the vulva and extended into the uterus without resistance. Foul-smelling and dark reddish-brown fluid dripped out of the catheter, and the fluid was collected. Transrectal ultrasonography was performed to guide the hysteroscope through the cervix. The cervix was not visualized on ultrasound, suggesting a fully dilated cervix. Throughout the vagina until the uterine body, which is the limit of the rectal probe (~45 cm), the lumen of the reproductive tract appeared deflated with no significant amount of fluid. Hysteroscopy was then used to view the internal structure of the reproductive tract. The vaginal and uterine walls were inflamed with copious amounts of debris and dark reddish fluid (**Figure 3B**).
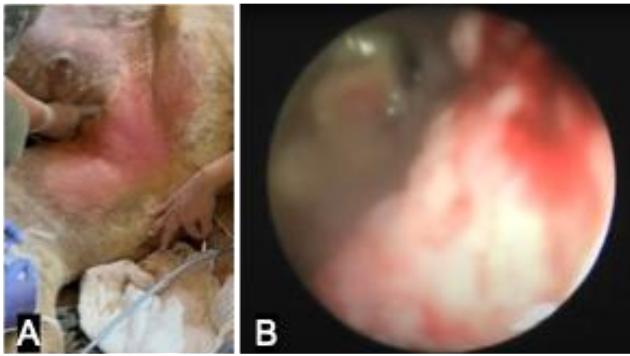
Figure 3 Clinical evidence observed in Lala, a 5-year-old female white lion (*Panthera leo*), managed in captivity in Zoo Melaka. (A) Cellulitis observed around the inguinal area; (B) Hysteroscopy shows the inflammation of the uterine wall with copious amounts of dark reddish fluid and debris.

An abdominal ultrasound was performed concurrently to locate remnants of fetuses in the reproductive tract, and no remaining fetuses were detected. Povidone-iodine was diluted with normal saline to a concentration of 1% and used to flush out debris and discharge from the uterus. Approximately 900mL of this dilution was used. The uterus was further flushed with saline (approximately 2 L) until the mucosa was clearly visible. Finally, 200mL of metronidazole (Metrogyl®, 5 mg/mL; Unique Pharmaceuticals, India) was infused into the uterus to help terminate the infection. During sedation, amoxycillin (Betamox LA®, Norbrook 150) 10mL, meloxicam (Melonex® 5 mg/mL, Intas Pharmaceuticals Ltd., India) 6mL, and multivitamin (Vitavet®, Nova) 15mL were administered. Fluids were administered subcutaneously and intravenously in a total volume of 3 L. Anaesthesia was reversed with yohimbine (Yohimbe®, Equimed, USA) 6mL, half IV and half IM. The patient's recovery was smooth and uneventful. The lioness regained her appetite immediately after food was offered and returned to estrus the following month.

Zoo Negara
Case 4

Manja is a 17-year-old female leopard (*Panthera pardus*) kept in Zoo Negara, Malaysia. The animals were housed with melanistic conspecifics. The leopard was slightly dull and inactive, and had a distended abdomen. Purulent vulvular discharge was observed upon closer examination under sedation. Radiography revealed that the intestines were craniodorsally displaced and there was a tubular structure with soft tissue radiopacity (**Figures 4A**, **B**). Abdominal ultrasonography revealed a distended uterus filled with fluid (**Figure 4C**). The animal was diagnosed with open pyometra. Complete blood count and serum biochemistry analysis revealed hyperproteinaemia and hyperglobulinemia. The culture results of vulvular discharge are shown in **Table 1**.

A ventral midline ovariohysterectomy was performed. General anesthesia was achieved with a combination of ketamine (Narketan®-10, Vetoquinol, UK,3.5 mg/kg) and xylazine HCl (Ilium Xylazil®, Troy Lab, Australia, 1 mg/kg). Fluid therapy (lactated Ringer's solution and Duphalyte®) was administered intravenously at a rate of 10 ml/kg/hr. Anti-
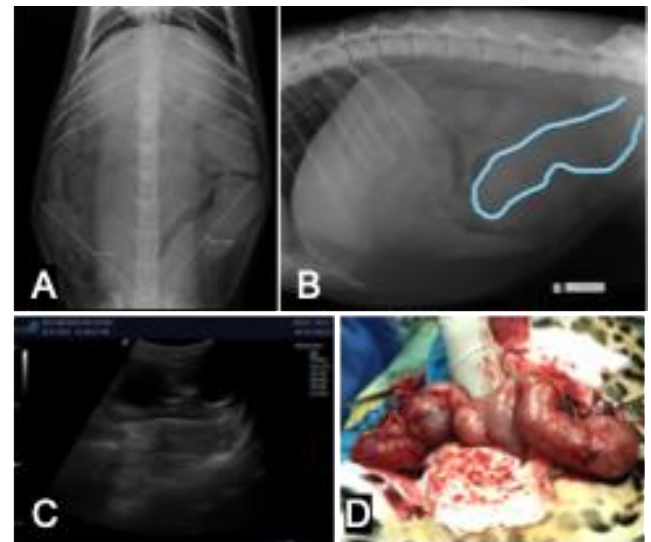

Figure 4 Clinical symptoms observed in Manja, a 17-year-old female leopard (*Panthera pardus*) kept in Zoo Negara, Malaysia**.** (A) Radiography imaging shows a tubular structure with soft tissue radiopacity; (B) Craniodorsally displaced intestines; (C) Ultrasonography imaging shows anechoic enlargement of the uterus; (D) A distended uterus observed during the ovariohysterectomy procedures.

inflammatory, multivitamin, and liver protectants were administered. The distended uterus (**Figure 4D**) was sent for histopathological examination and bacterial culture. The results revealed a uterine adenocarcinoma associated with an important growth of *Escherichia coli* and *Staphylococcus aureus* (**Table 6**). Antibiotics (enrofloxacin at a dosage of 5 mg/kg daily were replaced with amoxicillin and clavulanic acid at a dosage of 10 mg/kg LA, and meloxicam at a dose of 0.2 mg/kg was administered post-operatively every other day for about two weeks. The leopard recovered completely after surgery. However, the adenocarcinoma metastasized to the lungs, resulting in the death of the animal three months later.

National Wildlife Rescue Center
Case 5

Chemon is a 20-year-old female Malayan tiger (*Panthera tigris jacksoni*) managed in captivity at the National Wildlife Rescue Center (NWRC). The animals were housed individually and were not included in any breeding program. The animal was reported to have intermittent, bloody, and purulent vulvular discharge. The discharge was observed as a few spots on the night stall floor (**Figure 5A**). In addition, the animal was in good condition.

The tiger was fasted for 24 h before further examinations were performed. General anaesthesia was achieved using a combination of ketamine HCl (Ilium Ketamil®, Troy Lab, Australia, 3 mg/kg) and detomidine (Dormosedan®, Zoetis, USA, 0.07 mg/kg). Abdominal radiography revealed no significant findings. However, an abdominal ultrasound revealed a fluid-filled uterus. The dilatation of tubular structures ventral to the bladder with an anechoic appearance (**Figure 5B**) indicated pyometra. Swabs from the vagina were sent for bacterial isolation and antibiotic sensitivity tests, which revealed Haemolytic *E. coli* (**Table 1**). Vaginal cytology showed the presence of parabasal and intermediate cells with white blood

cells (WBC). All blood parameters were within the normal ranges. Amoxicillin at a dosage of 10 mg/kg was administered daily for 14 days. No discharge was observed after treatment.

Two months after treatment, the animal succumbed to clinical signs of inappetence, dullness, and lethargy. Bloody mucopurulent vulvular discharge was observed on the floor on the second day of observation. Treatment with Penicillin-streptomycin at a dosage of 10 mg/kg and SID for 14 days was initiated, followed by enrofloxacin at a dosage of 5 mg/kg in drinking water for 30 days. *E. coli* was isolated from the discharge (**Table 1**).
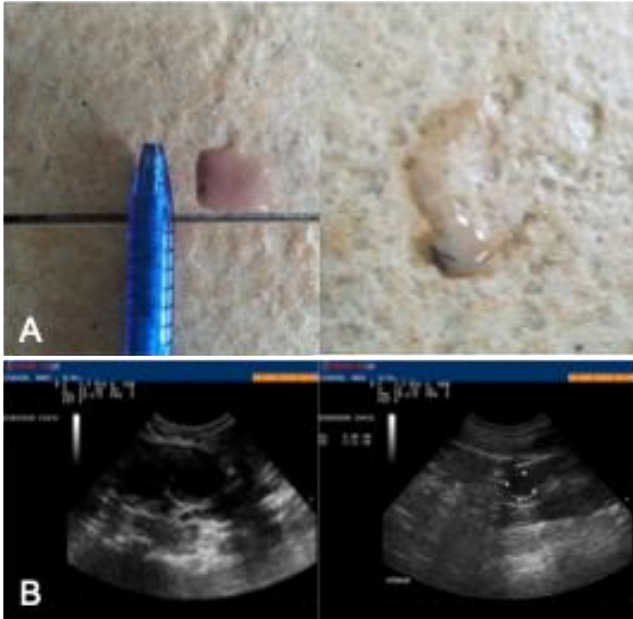

Figure 5 (A) Bloody mucopurulent vulvular discharge on the night stall floor was discharged by Chemon, a 20-year-old female Malayan tiger (*Panthera tigris jacksoni*) in captivity at the National Wildlife Rescue Center (NWRC), Malaysia; (B) Fluid-filled uterus revealed by ultrasonography.

The animal was scheduled for hysteriscopic examination 10 months after the second treatment session. Unfortunately, examination revealed a distended uterine body on both sides of the normal ovary. Mucopurulent vulvar discharge oozed out of the vulva as the animal was positioned throughout the procedure. Discharge was sent for bacterial culture and antibiotic sensitivity tests, which showed the presence of *Enterobacter* sp. (**Table 1**). Treatment with long-term antibiotics based on the antibiotic sensitivity test and prostaglandin F2 alpha (PGF2α) to facilitate expulsion of uterine content is intended.

Case 6

Mek Terapai is an approximately 18-year-old, wild-caught female Malayan tiger (*Panthera tigris jacksoni*). The animals were kept individually with 19 other tigers at NWRC. She was reported to have decreased appetite and a gradual loss of body weight. Before the procedure, the tiger was fasted for 24 hours. General anesthesia was achieved using a combination of ketamine HCI (Ilium Ketamil®, Troy Lab, Australia, 3 mg/kg) and detomidine (Dormosedan®, Zoetis, USA, 0.07 mg/kg).

Upon sedation, physical examination revealed anisocoria, a fair body score (2.5/5), and a 10 kg loss of body weight. Abdominal palpation revealed a hard mass. The animal was then subjected to radiography and ultrasonography. Abdominal radiography showed the presence of a radiopaque mass caudal to the left kidney and cranial to the bladder (**Figure 6A**). Through ultrasound, a mass of mixed echogenicity with a diameter of 9.4 cm x 9 cm was scanned (**Figure 6B**). Based on these findings, leiomyomas were highly suspected. Surgical treatment is not an option because of the high risk of prolonged anesthesia as the animal ages. Treatment was administered to alleviate the pain. Meloxicam (0.2 mg/kg and ranitidine (3 mg/kg) were administered PO and SID, respectively, for 7 days and repeated when necessary. The animal was cared for until her quality of life had decreased. The animals were then euthanized.
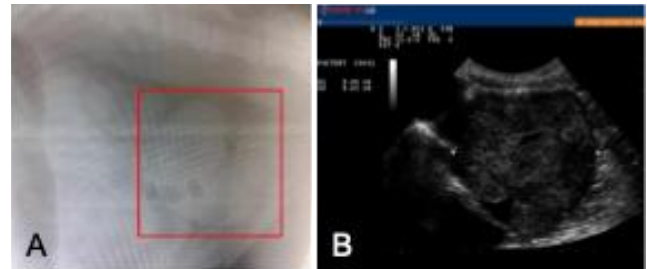

Figure 6 (A) Mass inside abdominal cavity, caudal to the left kidney and cranial to the bladder; (B) Mass inside abdominal cavity of Mek Terapai, an 18-year-old female Malayan tiger (*Panthera tigris jacksoni*) in captivity at the National Wildlife Rescue Center (NWRC), Malaysia.

Case 7

Tanjung is a 17-year-old Malayan tiger (*Panthera tigris jacksoni*) managed in captivity at the NWRC. The animal was kept with male conspecifics. The animal was reported to have intermittent smelly mucopurulent vulvular discharge. The discharge was observed on the night stall floor (**Figure 7A**), and a swab of the discharge was sent for bacterial isolation and antibiotic sensitivity testing, which revealed Haemolytic *E. coli* (**Table 1**). Otherwise, the animal was in good condition. Before further diagnostics were performed, the tiger was fasted for 24 hours before general anesthesia. A combination of ketamine HCI (Ilium Ketamil®, Troy Lab, Australia, 5 mg/kg) and detomidine (Dormosedan®, Zoetis, USA, 0.07 mg/kg) was given.

Abdominal ultrasound revealed bilateral anechoic uterine horns measuring 4.64 x 3 cm. The uterine body (2.69 cm was filled with anechoic fluid (**Figure 7B**), indicating pyometra. Swabs from the vagina were sent for bacterial isolation and antibiotic sensitivity testing, which revealed E. coli (**Table 1**). Vaginal cytology revealed Numerous PMNs and a mixture of nucleated and anucleated superficial cells. The blood parameter revealed an increase in eosinophils. Treatment with amoxicillin and clavulanic acid at a dosage of 12.5 mg/kg was administered for 30 days, a luteolytic agent (PGF2alpha) at a dosage of 1μg/kg was given for 4 days, and the dosage was increased to 2μg/kg for another 3 days. This is because no effect was observed at a lower dosage. No discharge was observed after treatment.

Table 1 Comparative details of all uterine disease cases reported in the present case study

Details	Captivity and Case						
	Sunway Lagoon Wildlife Park		Zoo Melaka	Zoo Negara	National Wildlife Rescue Center		
	Case 1: white Bengal tiger	Case 2: white lion	Case 3: White lion	Case 4: leopard	Case 5: Malayan tiger	Case 6: Malayan tiger	Case 7: Malayan tiger
Age	8 years	8 years	5 years	17 years	20 years	~18 years	17 years
Housing	with male conspecific	with male conspecific	with male conspecific	with male conspecific	individual	individual	with male conspecifics
Clinical Signs	Weakness, acute bloody vulvar discharge with mucus	Milky caseous/watery discharge, hyporexia, dullness, vomiting	Inappetence, expulsion of dead fetuses, dark foul-smelling vaginal discharge, lateral recumbency	Dullness, inactivity, distended abdomen, purulent vulvular discharge	Intermittent bloody, purulent vulvular discharge	hyporexia, gradual weight loss	Intermittent smelly mucopurulent vulvular discharge
Radiography Findings	N/A	N/A	N/A	Intestines craniodorsally displaced; tubular structure with soft tissue radiopacity	No significant findings	Radiopaque mass caudal to left kidney and cranial to bladder	N/A
Ultrasound Findings	N/A	Fluid-filled tubular structures	Uterine body deflated; no significant fluid; no remaining fetuses	Distended uterus filled with fluid (anechoic)	Fluid-filled uterus; dilatation of tubular structures (anechoic)	Mass of mixed echogenicity	Bilateral anechoic uterine horns with filled with anechoic fluid
Blood Parameters	Neutrophilia, leukocytosis, lymphopenia, high PCV/Hb, thrombocytopenia, hypoglycemia, low BUN, hyperproteinemia, hyperglobulinemia, high ALT/amylase/lipase	Leukocytosis with neutrophilia and monocytosis	Neutrophilia, monocytosis, increased creatinine, hyperglobunemia	Hyperproteinemia, hyperglobulinemia	Within normal ranges	N/A	Eosinophilia
Bacterial Culture Findings	*Eschericia coli*, *Enterococcus faecalis*	*Eschericia coli*, *Proteus* sp.	*Eschericia coli*	*Eschericia coli*, *Staphylococcus aureus*, *Proteus* sp.	Haemolytic *Eschericia coli*, *Enterobacter* sp.	N/A	Haemolytic *E Eschericia coli*, *Enterococcus* sp., *Staphylococcus* sp.
Susceptible Antibiotics	Gentamicin, Augmentin	Azithromycin, Doxycycline, Gentamicin, Imipenem, Marbofloxacin, Septrin, Augmentin, Cefovecin, Ceftriaxone	Ampicillin, Augmentin, Cefuxine, Ceftriaxone, Gentamicin, Imipanem	Amoxicillin/Clavulanic Acid, Cefuroxime, Enrofloxacin	Fosfomycin, Cefotaxime, Ciprofloxacin, Chloramphenicol, Ceftiofur, Tetracycline, Enrofloxacin, Gentamicin	N/A	Colistin, Cefotaxime, Ciprofloxacin, Ceftiofur, Gentamicin, Chloramphenicol
Resistant Antibiotics	Penicillin G, Enrofloxacin	Amoxicillin, Enrofloxacin, Metronidazol, Clindamycin, Doxycycline, Septrin	Amoxicillin, Ampicillin/Sulbactam, Ciprofloxacin, Sulp/Trimethoprim	Amoxicillin, Doxycycline, Metronidazol, Ampicillin, Enrofloxacin	Erythromycin, Penicillin	N/A	Tilmicosin, Ampicillin, Erythromycin, Trimethoprim/Sulphamethaxole
Diagnosis	Ulcerative endometritis, polycystic ovaries	Pyometra	Post-parturition uterine infection/inflamed uterine walls	Pyometra; uterine adenocarcinoma	Pyometra	Suspected Leiomyoma	Pyometra; perforation of uterus (post-mortem)

| Details	Captivity and Case						
	Sunway Lagoon Wildlife Park		Zoo Melaka	Zoo Negara	National Wildlife Rescue Center		
	Case 1: white Bengal tiger	Case 2: white lion	Case 3: white lion	Case 4: leopard	Case 5: Malayan tiger	Case 6: Malayan tiger	Case 7: Malayan tiger
Treatments	Enrofloxacin, Meloxicam, Amoxicillin, Vitamin K, Ranitidine, Cloprostenol	Amoxicillin/Clavulanic acid, Marbofloxaci, Cloprostenol, Meloxicam, Catosal, Ivermectin	Marbofloxacin, Amoxicillin, Meloxicam, Cloprostenol, Metronidazole (infusion)	Enrofloxacin, Amoxicillin/Clavulanic acid, Meloxicam, Multivitamin, Liver protectants	Amoxicillin, Penicillin-streptomycin, Enrofloxacin, Cloprostenol	Meloxicam, Ranitidine	Amoxicillin/Clavulanic acid, Cloprostenol
Outcome	Died 4 days after surgery	Recovered	Smooth recovery; returned to estrus the following month	Recovered from surgery; died 3 months later due to lung metastasis	Recovered	Euthanized	Died ,post-mortem revealed uterine perforation

N/A: not applicable
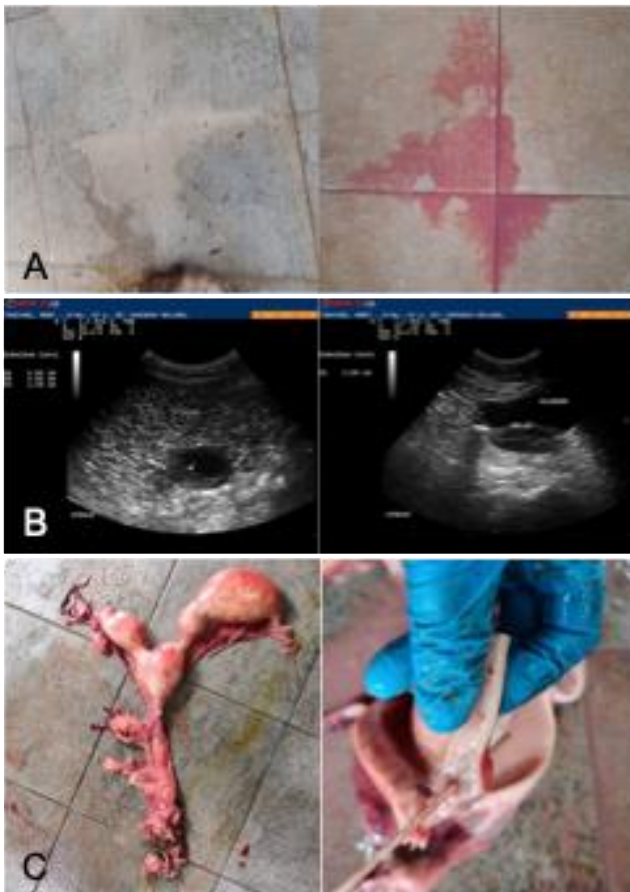
Figure 7 (A) Mucopurulent vulvular discharge in the night stall floor of Tanjung, a 17-year-old female Malayan tiger (*Panthera tigris jacksoni*) in captivity at the National Wildlife Rescue Center (NWRC), Malaysia; (B) Fluid-filled uterus confirmed by ultrasonography; (C) Uterus with pyometra and perforation of the uterus.

Two months after treatment, the animal exhibited behavioral changes, where it became more aggressive and was inappetent for 2 days before it was found dead. A post-mortem examination revealed perforation of the uterus as a sequela of a long-standing clinical case of pyometra (**Figure 7C**). The uterine sample was sent for bacterial isolation and histology, which demonstrated *Enterococcus* sp. and *Staphylococcus* sp. The histology of the uterus showed squamous epithelium layer hyperplasia with a large number of lymphocytes and plasma cells in the endometrial stroma. The vulva showed thickening of stratified squamous epithelium.

Discussion

In six out of the seven case reports, the animals were eight years of age or older. This age distribution is consistent with previous findings indicating an increased risk of reproductive pathology with advancing age. In a study in cheetahs, roughly 30% of females aged two to four years had developed cystic endometrial hyperplasia (CEH), and over 80% of females older than five years were affected (Crosier *et al.*, 2011). Another study in domestic cats also found that the incidence of CEH increases drastically with age (Binder *et al.*, 2021). A study evaluating the frequency of neoplasms in captive wild felids in southern Italian zoos reported that affected animals ranged from six to nineteen years of age, although the neoplasms were not specific to the reproductive system (d'Aquino *et al.*, 2022). Collectively, these findings emphasize the importance of routine uterine and reproductive assessments in female felids from approximately six years of age onward.

In five cases, the animals were housed with male conspecifics, whereas in the remaining two cases, male tigers were kept in the same building. In addition, three of the seven animals had a history of abortion or stillbirth. Although the sample size is limited, this observation suggests a possible association between previous reproductive events and uterine pathology, warranting further retrospective investigation.

A previous retrospective study examining 212 reproductive tracts of female zoo felids identified an increased risk of pyometra development in animals treated with melengestrol acetate (MGA) contraceptives (14 of 26 affected animals had received MGA). Furthermore, adenomatous and cystic hyperplasia was present in 85% of MGA-treated animals (Munson *et al.*, 2002). In contrast, none of the animals in the present study had received contraceptive treatment, indicating that

uterine disease may also develop independently of hormonal intervention.

The use of contraceptives in captive felid management was first reported in the 1970s. Their benefits include population control, genetic management, welfare and social stabilization, and reduction of prolonged progesterone exposure in non-pregnant females (Guthrie *et al*., 2021). Current recommendations favor the use of gonadotropin-releasing hormone (GnRH) agonists such as deslorelin acetate (DA), which show high efficacy in preventing pregnancy (Guthrie *et al*., 2021). Unlike synthetic progestins such as MGA, DA has not been associated with reproductive pathology (Cowl *et al*., 2018; Moresco & Agnew, 2013). However, further data collection is required to establish best-practice guidelines for long-term DA use in zoo felid populations. Female felids, particularly spontaneous ovulators not included in breeding programs or of advanced age, should be considered potential candidates for contraception.

The most common clinical sign observed was vulvular discharge (mucopurulent, bloody, or malodorous), present in six cases. Reduced appetite or inappetence was observed in five cases, followed by dull appearance in four cases. Polyuria and polydipsia were not observed, consistent with previous reports (McCain *et al*., 2009).

Escherichia coli was the most frequently isolated microorganism, identified in 8 of 11 vulvular swab cultures, followed by hemolytic *E. coli* and *Proteus* spp. (2 of 11 each). This aligns with previous findings identifying *E. coli* as the predominant pathogen in uterine infections of small animals and wild felids (Feldman, 2000; McCain *et al*., 2009)..

Based on antimicrobial susceptibility testing, gentamicin was the most reliable antibiotic for *E. coli* isolates (susceptible in 6 of 8 cultures), followed by azithromycin, marbofloxacin, ceftiofur, cefuroxime, and chloramphenicol (each susceptible in 2 of 7 cultures). Hemolytic *E. coli* isolates were susceptible to gentamicin, ceftiofur, and chloramphenicol (2 of 2 cultures). *Proteus* spp. isolates were susceptible to amoxicillin–clavulanic acid (2 of 2 cultures). These findings underscore the importance of culture and sensitivity testing to guide rational antimicrobial use.

Common hematological and biochemical abnormalities included leukocytosis, neutrophilia, hyperproteinemia, and hyperglobulinemia, observed in five of seven cases. These findings are consistent with inflammatory responses observed in pyometra in domestic carnivores and large felids (Feldman, 2000; McCain *et al*., 2009). Ultrasonography proved to be a reliable diagnostic modality compared with radiography, revealing bilateral enlargement of uterine horns with anechoic or mixed echogenic contents in five cases, consistent with pyometra.

The decision to manage each case medically or surgically depends on two main factors. The factors included the age and clinical presentation of the animals. Old animals pose a high risk of anesthesia, whereas younger animals still have reproductive potential. In these cases, a medical approach with antibiotics and luteolytic agents may be more suitable, as seen in five out of seven cases. However, it must be noted that in cases of pyometra, recurrence was observed in three

out of four medically treated cases reported here, highlighting the limitations of conservative therapy. Surgical intervention remains the definitive treatment to remove infection and neoplastic tissue, particularly in clinically compromised animals. However, postoperative management in wildlife remains challenging. In domestic cats, the ventral midline approach is associated with higher wound complication rates compared with the flank approach (Roberts *et al*., 2015). In the present study, suture breakdown occurred in both cases undergoing midline ovariohysterectomy, suggesting that flank or minimally invasive approaches may be preferable. A lateral flank approach for ovariohysterectomy reduces the risk of evisceration and promotes better wound healing (Yun *et al*., 2021). A laparoscopic–assisted ovariohysterectomy for treatment of pyometra has been described in a Bengal Tiger (Rainey *et al*., 2018). Although this method is new and not fully developed for the treatment of pyometra, the reduction in incision size was desirable as incisional complications are difficult to assess and treat in large, exotic felids.

Out of the seven cases, three animals (one white tiger, one white lion, and one leopard) were anesthetized with ketamine and xylazine, followed by all three Malayan tigers using ketamine and detomidine, with one white lion using the combination of ketamine, xylazine, and tiletamine zolazepam. Ketamine hydrochloride remains the most commonly chosen drug due to its safety and efficiency in a wide range of wildlife (Cushing, 2025). The drug is often paired with alpha-2 agonists such as xylazine and detomidine to minimize side effects like seizures, muscle stiffness, and rough recovery. The addition of alpha-2 agonists allows the effects of the drugs to be reversible, resulting in smoother and quicker recoveries in animals (Cushing, 2025).

Newer alpha-2 agonists, such as medetomidine, are widely used in large felids; however, they were not used in these cases due to availability issues. Xylazine, while readily available in the region, poses a risk of respiratory depression and requires close monitoring during procedures. Fortunately, these effects were not observed in the anesthesia of the cases, except for seizures in the white tiger, which were managed with diazepam.

Benzodiazepines can also be incorporated into the protocol to reduce the risk of seizures and promote muscle relaxation. Due to varied absorption rates and the painful nature of injections, midazolam is more commonly used compared to diazepam (Cushing A, 2025). In all cases, the anesthesia was maintained with injectable anesthetics due to the field location of the procedures. Inhalant anesthesia would be preferred for longer procedures, as tidal concentrations can be adjusted according to the required plane and depth of anesthesia.

The use of butorphanol-azaperone-medetomidine (BAM) in wildlife is gaining attention. Reports on BAM use in cheetahs and African lions indicated rapid induction and recovery with no adverse effects (Semjonov *et al*., 2017, 2019).

Conclusion

Uterine diseases have been increasingly reported in female captive large felids. Any intact female large felids over the

age of 8 years that are lethargic and anorexic, with or without vulvular discharge, should be examined for uterine diseases using ultrasonography and blood work-up. Reproductive evaluation of large captive felids should be included in annual health checks as the females age. The usage of contraceptives as an option to reduce the risks of developing uterine diseases in older females should also be further developed as a part of long-term reproductive management for captive felids.

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